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Poster Abstract: Therapeutic

Long-Term Follow-Up of Two Siblings with a Non-Classic Infantile Variant Form of Pompe Disease

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BACKGROUND

Enzyme replacement therapy (ERT) is effective in prolonging survival and improving cardiomyopathy and motor outcomes in patients with Pompe disease (PD). Factors influencing response to therapy include age at onset, genotype, extent of pathology, and muscle damage at the time of starting treatment.[1]

CASE REPORTS

We report on two siblings, a sister and brother, with a non-classic infantile variant of PD on ERT for 9 years, and compare their clinical outcome and muscle MRI findings.

Both siblings were heterozygote for two mutations c.572A>G (p.Glu176fsX)/c.525delT (p.Tyr191Cys) of the GAA gene.[2] The sister (Patient 1) received the diagnosis at the age of 4 years, because of facial weakness, rhinolalia, limb girdle muscular weakness, walking, climbing, and jumping difficulties, and hyperCPKemia. Echocardiography revealed hypertrophic cardiomyopathy (LVMI 177.8 g/m^2). Diagnosis was confirmed by assessment of GAA activity in muscle biopsy, resulting in an undetectable level. The brother (Patient 2) has been evaluated at 7 months of age soon after the diagnosis of his sister. Physical examination was normal, but hyperCPKemia and hypertrophic cardiomyopathy (LVMI 150 g/m^2) were recorded. GAA activity in leukocytes was undetectable. Both siblings initiated ERT as compassionate therapy at 4.6 years (Patient 1) and 18 months (Patient 2) of age. Cardiac hypertrophy disappeared within 2 years in Patient 1 and 1 year in Patient 2. ERT has been well tolerated and no increase in anti-rhGAA antibodies has ever been detected.

During long-term follow-up, Patient 2 has maintained a completely normal motor function and at the age of 10 years, he has no signs of myopathy.

Patient 1, now 13 years old, has shown progressive muscular weakness with a marked steppage gait. At the 6-minute walk test, she covered a distance of 480 m. She has never acquired the ability to jump and run. Functional pulmonary test showed a progressive chronic respiratory insufficiency (FEV1 65%).

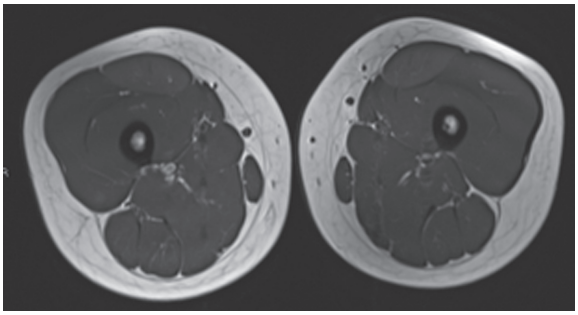

Fig. 1.

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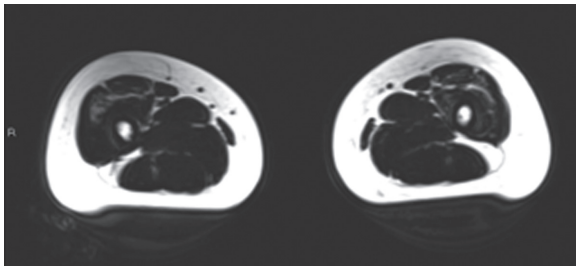

Fig. 2.

After 9 years of ERT, muscle MRI was performed on a 3T Siemens scanner in both patients.

Patient 2 did not show any significant or selective fat infiltration in all examined muscle on T1 images (Fig. 1). T2 STIR image showed mild hyperintensity of muscle rectus bilaterally, interpreted as muscle edema.

Patient 1 showed, in both quadriceps, a slight T1 hyperintensity, due to fat substitution (Fig. 2), and, to a greater extent, marked T1 hyperintensity of the tongue. No impairment of the scapular and pelvic girdle, or paravertebral muscles was evident. T2 STIR images showed diffuse, bilateral and symmetrical muscle edema in the gluteus maximus, quadriceps and the posteromedial compartment of the thigh.

CONCLUSIONS

These different outcomes in two siblings confirm that an early start of ERT in PD is effective in preventing progression of the disease, in particular of muscle damage.

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